

**CLAIMS**

1. A substantially pure consecutive and anti-angiogenic polypeptide, comprising the central  
5 region of human histidine rich glycoprotein (HRGP) corresponding to SEQ.ID.NO:2.
2. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a  
subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment  
corresponding to region 330-364 (SEQ.ID.NO:1) of mature human HRGP.  
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3. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 2, said  
subfragment having an amino acid length of between 3 and 35 amino acids.
4. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 3,  
15 having an amino acid length selected from the group consisting of between 3 and 25 amino  
acids, 3 and 20 amino acids, 3 and 15 amino acids, 3 and 10 amino acids, and 3 and 8  
amino acids.
5. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a  
20 subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment  
corresponding to SEQ.ID.NO:18.
6. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a  
subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment  
25 corresponding to SEQ.ID.NO:17.
7. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 6,  
wherein said polypeptide comprises an additional glycine (G) residue in the C-terminal end  
(residue 26) of said polypeptide, said polypeptide corresponding to SEQ.ID.NO:16.  
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8. A substantially pure consecutive and anti-angiogenic polypeptide comprising a subfragment  
of the central region of human HRGP (SEQ.ID.NO:2), said subfragment corresponding to  
SEQ.ID.NO:22.
- 35 9. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 8,  
wherein said polypeptide is modified through an acetylation and/or an amidation in the N-  
terminal, and/or C-terminal end, said polypeptide corresponding to SEQ.ID.NO:21.
- 40 10. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a  
subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment  
corresponding to SEQ.ID.NO:24.

11. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 10, wherein said polypeptide is modified through an acetylation and/or an amidation in the N-terminal and/or C-terminal end, said polypeptide corresponding to SEQ.ID.NO:23.
- 5 12. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment corresponding to SEQ.ID.NO:26.
- 10 13. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 12, wherein said polypeptide is modified through an acetylation and/or an amidation in the N-terminal and/or C-terminal ends, said polypeptide corresponding to SEQ.ID.NO:25.
- 15 14. A substantially pure consecutive and anti-angiogenic polypeptide, comprising a subfragment of the central region of human HRGP (SEQ.ID.NO:2), said subfragment corresponding to SEQ.ID.NO:28.
- 20 15. A substantially pure consecutive and anti-angiogenic polypeptide according to claim 14, wherein said polypeptide is modified through an acetylation and/or an amidation in the N-terminal and/or C-terminal ends, said polypeptide corresponding to SEQ.ID.NO:27.
- 25 16. A substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims, wherein said polypeptide is isolated from human HRGP.
- 30 17. A substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims, wherein said polypeptide is isolated from proteolytically processed human HRGP purified from plasma.
- 35 18. A substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-15, wherein said polypeptide is recombinantly produced and/or isolated from recombinantly produced human HRGP.
- 40 19. A synthetically produced, substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-15.
20. A substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims, characterised in that it does not bind to thrombospondin.
21. A substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims, characterised in that it does not promote angiogenesis.

22. An anti-angiogenic pharmaceutical composition, comprising an effective amount of a substantially pure consecutive and anti-angiogenic polypeptide according to any of the preceding claims.
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23. An anti-angiogenic pharmaceutical composition according to claim 22, further comprising a pharmaceutically acceptable carrier.
24. An anti-angiogenic pharmaceutical composition according to any of claims 22-23, further comprising an anti-angiogenic agent.
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25. An anti-angiogenic pharmaceutical composition according to claim 24, wherein said anti-angiogenic agent is selected from the group consisting of angiostatin, thrombostatin, endostatin, interferon- $\alpha$ , interferon-inducible factor 10, and platelet factor 4.
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26. An anti-angiogenic pharmaceutical composition according to any of claims 22-25, further comprising an anti-neoplastic agent.
27. An anti-angiogenic pharmaceutical composition according to claim 26, wherein said anti-neoplastic agent is selected from the group consisting of taxol, cyclophosphamide, carboplatinum, cisplatin, cisplatin, gancyclovir, camptothecin, paclitaxel, hydroxyurea, 5-azacytidine, 5-aza-2'-deoxycytidine, and suramin.
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28. An anti-angiogenic pharmaceutical composition according to any of claims 22-27, further comprising an anti-inflammatory agent.
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29. An anti-angiogenic pharmaceutical composition according to claim 28, wherein said anti-inflammatory agent is selected from the group consisting of prednisone, a cox-2 inhibitor, ibuprofen and aspirin.
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30. An anti-angiogenic pharmaceutical composition according to any of claims 22-29, further comprising an effective amount of  $Zn^{2+}$ .
31. A substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for use as a medicament.
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32. Use of a substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for the manufacture of a medicament for the inhibition of angiogenesis in a mammal.
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33. Use of a substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for the manufacture of a medicament for treating and/or preventing cancer in a mammal.
- 5 34. Use of a substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for the manufacture of a medicament for inhibiting tumour growth in a mammal.
- 10 35. Use of a substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, for the manufacture of a medicament for treating and/or inhibiting myocardial angiogenesis, diabetic retinopathy, diabetic neovascularization, inappropriate wound healing, or an inflammatory disease in a mammal.
- 15 36. Use according to any of claims 32-35, wherein said mammal is a mouse.
37. Use according to any of claims 32-35, wherein said mammal is a rat.
38. Use according to any of claims 32-35, wherein said mammal is a human.
- 20 39. Method for inhibiting angiogenesis in a mammal, comprising administering a substantially pure consecutive and anti-angiogenic polypeptide according to any of claims 1-21 and/or a pharmaceutical composition according to any of claims 22-30, to a mammal in need thereof.
- 25 40. An isolated nucleic acid sequence that encodes a consecutive subfragment according to any of claims 1-21.
- 30 41. An expression vector comprising a nucleic acid sequence according to claim 40, optionally operatively linked to a promoter and/or additional regulatory sequences that regulate the expression of said nucleic acid sequence in a eukaryotic or prokaryotic host cell.
42. A host cell transformed and/or transfected with an expression vector according to claim 41.
- 35 43. A host cell according to claim 42, selected from the group consisting of mammalian cells, such as human, mouse or rat cells, and bacteria, yeast, and insect cells.
- 40 44. Method for inhibiting angiogenesis in a mammal, comprising administering an isolated nucleic acid according to claim 40, a host cell according to claim 42 or 43, and/or a vector according to claim 41 to a mammal in need thereof.